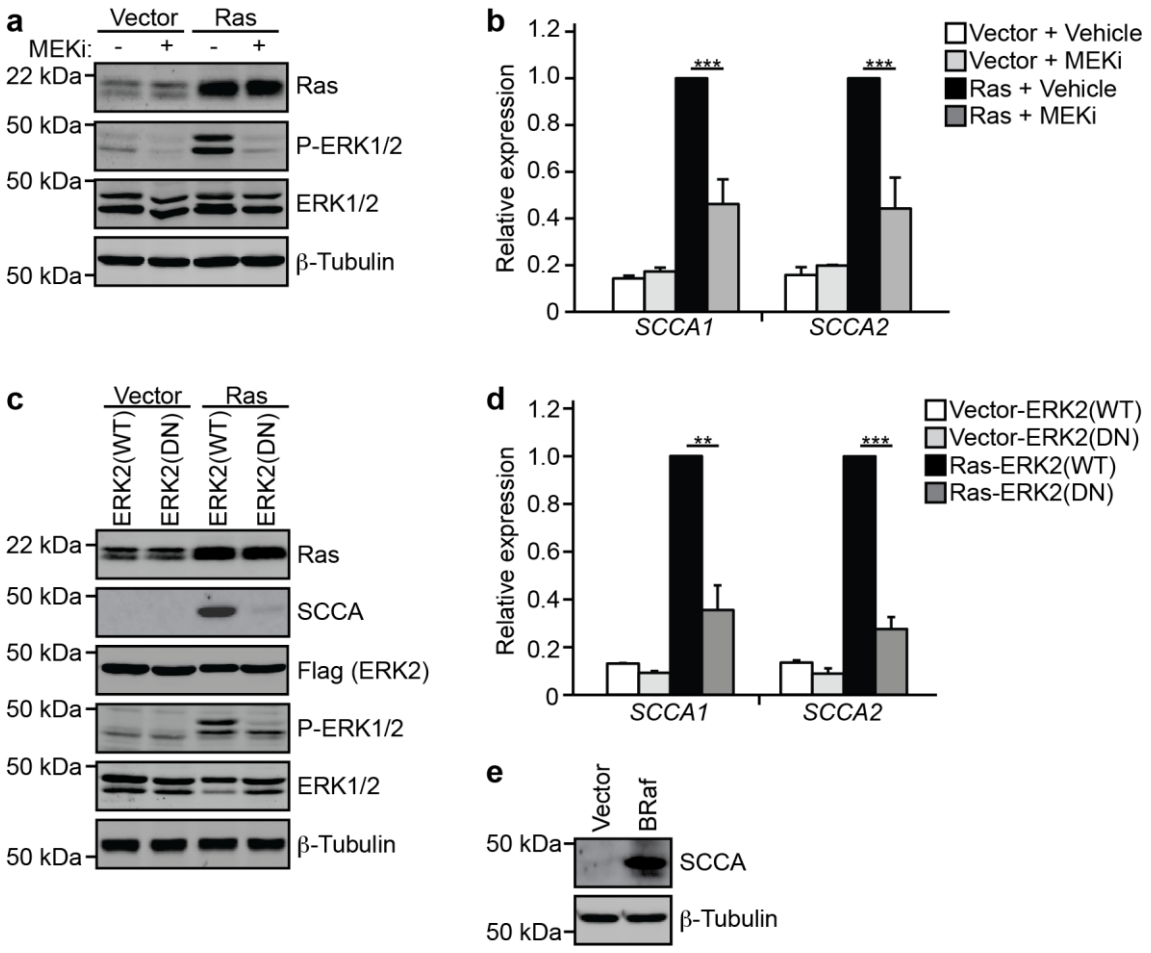
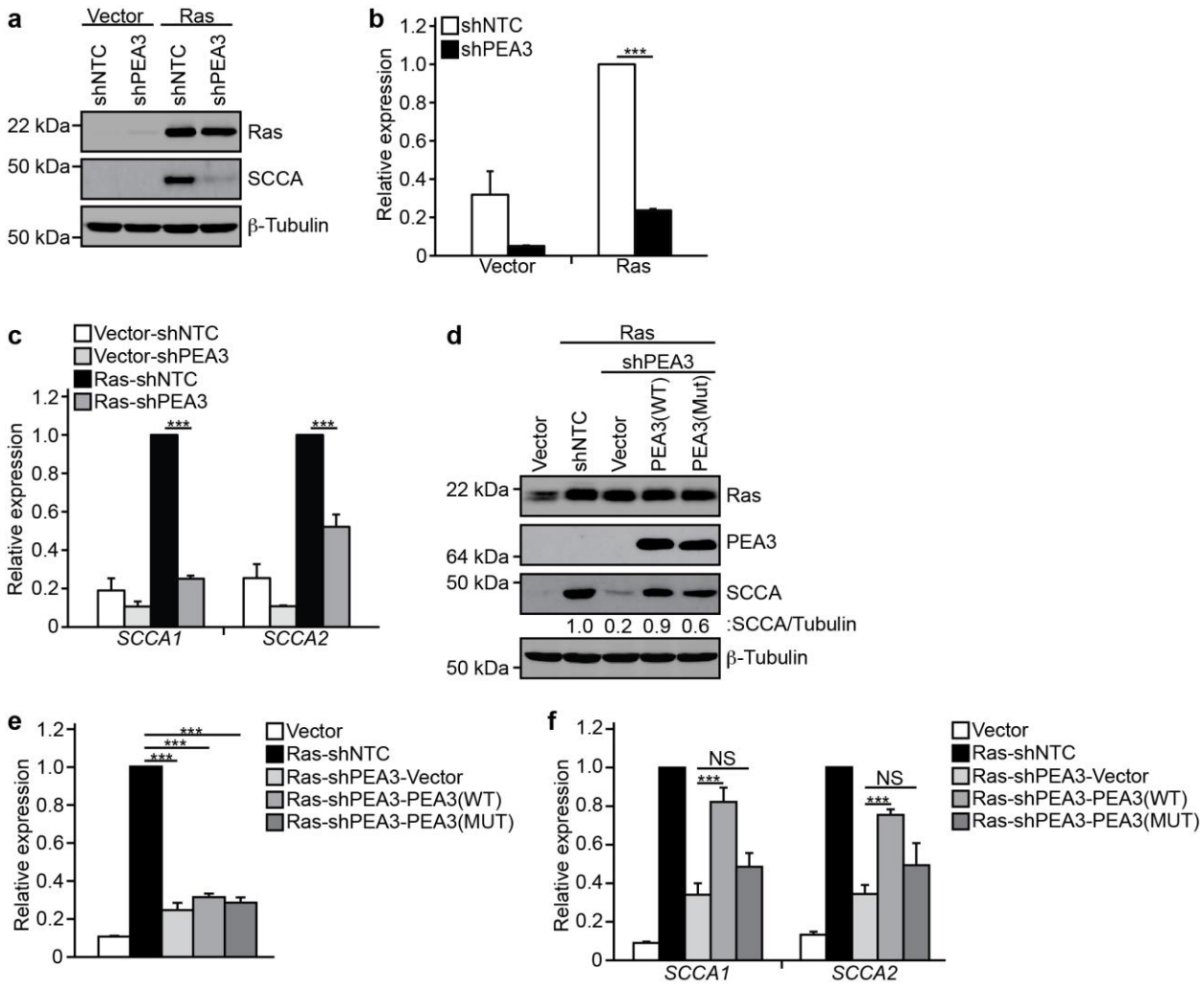


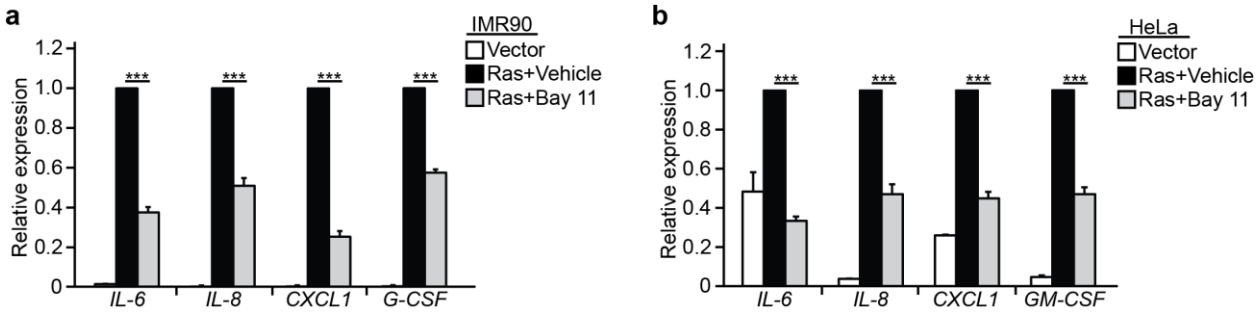
Supplementary Figure 1. Ras-induced SCCA expression is sensitive to the inhibition of MAPK in HeLa cells. (**a, b**) $KRas^{V12}$-expressing HeLa cells were treated with either vehicle control or U1026 (MEKi, 10 μM) for 24 h. (**a**) Whole cell lysates were analyzed by western blot with indicated antibodies. (**b**) Total RNA was extracted and SCCA1 and SCCA2 transcript levels were analyzed via qRT-PCR, and normalized to Ras^{V12} cells treated with vehicle control. Data shown are mean + SEM of two independent experiments performed in triplicate. (**c, d**) Vector-control or $KRas^{V12}$-expressing HeLa cells were transfected with either wild-type ERK2 (ERK2-WT) or dominant-negative ERK2 (ERK2-DN). (**c**) Whole cell lysates were analyzed by western blot with indicated antibodies. (**d**) Total RNA was extracted and SCCA1 and SCCA2

transcript levels were analyzed via qRT-PCR, and normalized to Ras^{V12}-ERK2(WT). Data shown are mean + SEM of two independent experiments performed in triplicate. **(e)** HeLa cells were stably transduced with either vector-control of $BRaf^{V600}$. Whole cell lysates were analyzed by western blot with indicated antibodies. **p<0.01; ***p<0.001 by t-test.

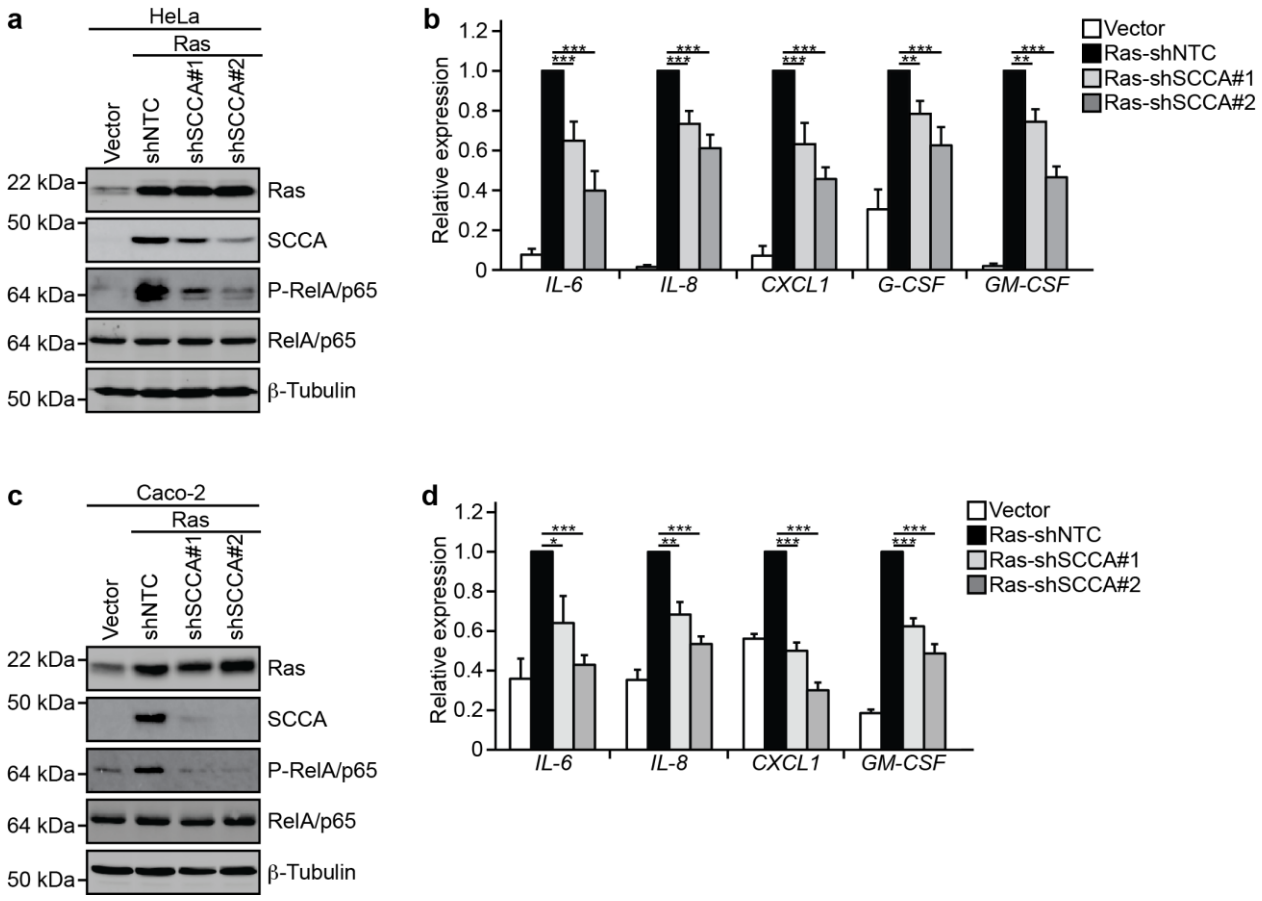


Supplementary Figure 2. Ras-induced SCCA expression is mediated by the ETS transcriptional factor PEA3. (**a-c**) Vector-control or $KRas^{V12}$-expressing HeLa cells were stably transduced with either shNTC or shPEA3. (**a**) Whole cell lysates were analyzed by western blot with indicated antibodies. (**b, c**) Total RNA was extracted and the transcript levels of (b) PEA3 and (**c**) SCCA1 and SCCA2 were analyzed via qRT-PCR. Transcript levels were normalized to Ras-shNTC cells. Data shown are mean + SEM of two independent experiments performed in triplicate. (**d-f**) $KRas^{V12}$-expressing HeLa cells were transiently transfected with either shNTC or shPEA3 and either vector-control, wild-type PEA3, or mutant PEA3. (**d**)

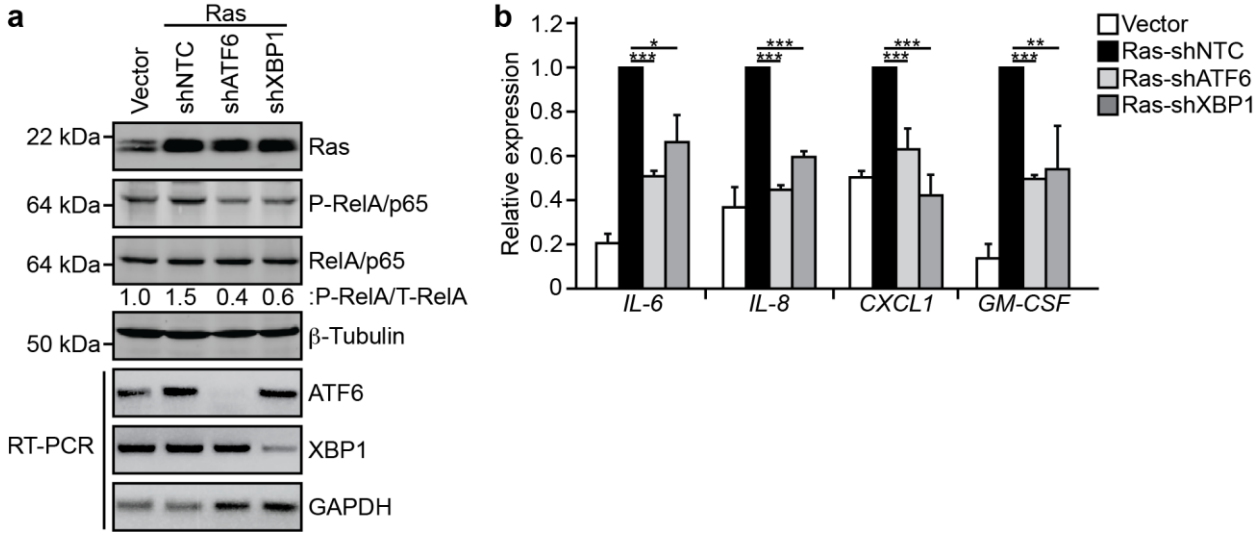
Whole cell lysates were analyzed by western blot with indicated antibodies. (**e, f**) Total RNA was extracted and the transcript levels of (**e**) PEA3 and (**f**) SCCA1 and SCCA2 were analyzed via qRT-PCR. Transcript levels were normalized to Ras-shNTC cells. Data shown are mean + SEM of two independent experiments performed in triplicate. ***$p<0.001$ by t-test; NS, non-significant by t-test.



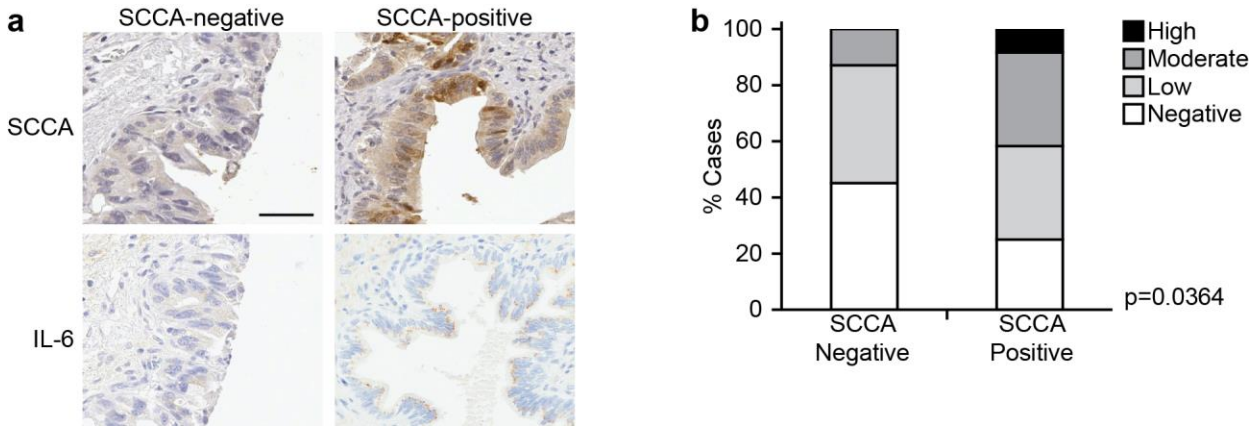
Supplementary Figure 3. Inhibition of NF-κB signaling abrogates Ras-induced cytokine production. (**a, b**) Vector-control or Ras^{V12}-expressing IMR90 (HRas) and HeLa (KRas) cells were treated with either vehicle control or the NF-κB inhibitor Bay-11-7082 for 16 hr. Total RNA was extracted and the transcript levels were analyzed via qRT-PCR. Transcript levels were normalized to Ras cells treated with vehicle control. Note: *GM-CSF* and *G-CSF* are not shown because their expression was not significantly altered with Bay-11-7082 treatment in IMR90 and HeLa cells, respectively. Data shown are mean + SEM of two independent experiments performed in triplicate. ***$p<0.001$ by t-test.



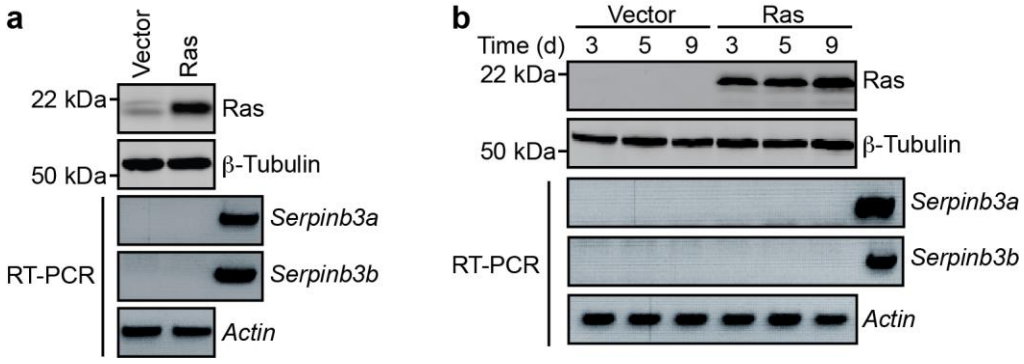
Supplementary Figure 4. SCCA silencing abrogates Ras-induced cytokine production. (**a-d**) Vector-control or $KRas^{V12}$-expressing HeLa and Caco-2 cells were stably transduced with either shNTC or two independent hairpins targeting SCCA. (**a, c**) Whole cell lysates were analyzed by western blot with indicated antibodies. (**b, d**) Total RNA was extracted and the transcript levels were analyzed via qRT-PCR. Transcript levels were normalized to Ras-shNTC cells. Note: For (**d**) *G-CSF* is not shown because it is not significantly up-regulated by $KRas^{V12}$. Data shown are mean + SEM of two independent experiments performed in triplicate. *p<0.05; **p<0.01; ***p<0.001 by t-test.



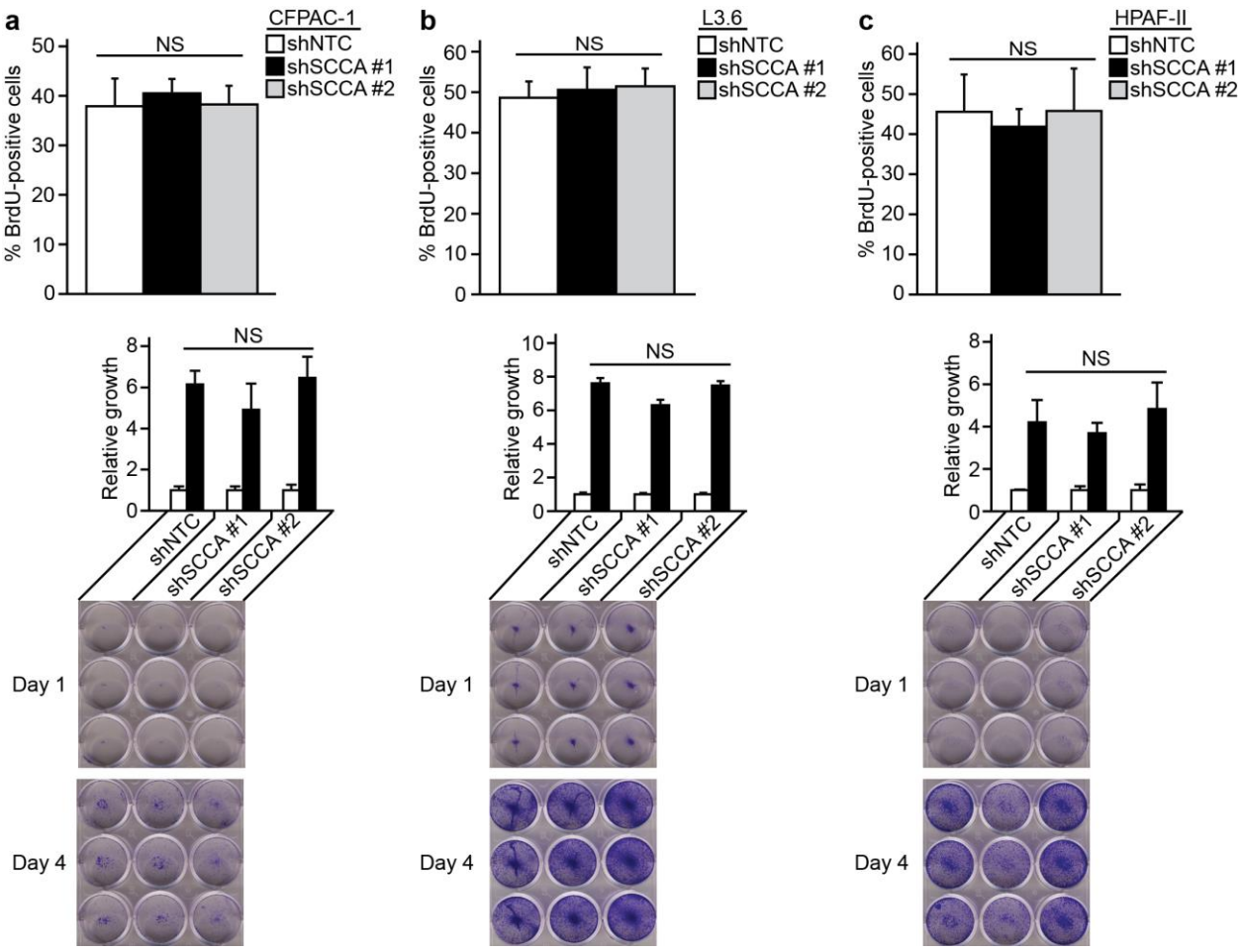
Supplementary Figure 5. Ras-induced cytokine production is mediated by an ER-stress response. (**a, b**) Vector-control or $KRas^{V12}$-expressing Caco-2 cells were stably transduced with either shNTC, shATF6, or shXBP1. (**a**) Whole cell lysates were analyzed by western blot with indicated antibodies. (**b**) Total RNA was extracted and the transcript levels were analyzed via qRT-PCR. Transcript levels were normalized to Ras-shNTC cells. Note: For (**b**) *G-CSF* is not shown because it is not significantly up-regulated by $KRas^{V12}$. Data shown are mean + SEM of two independent experiments performed in triplicate. *p<0.05; **p<0.01; ***p<0.001; NS, non-significant by t-test.



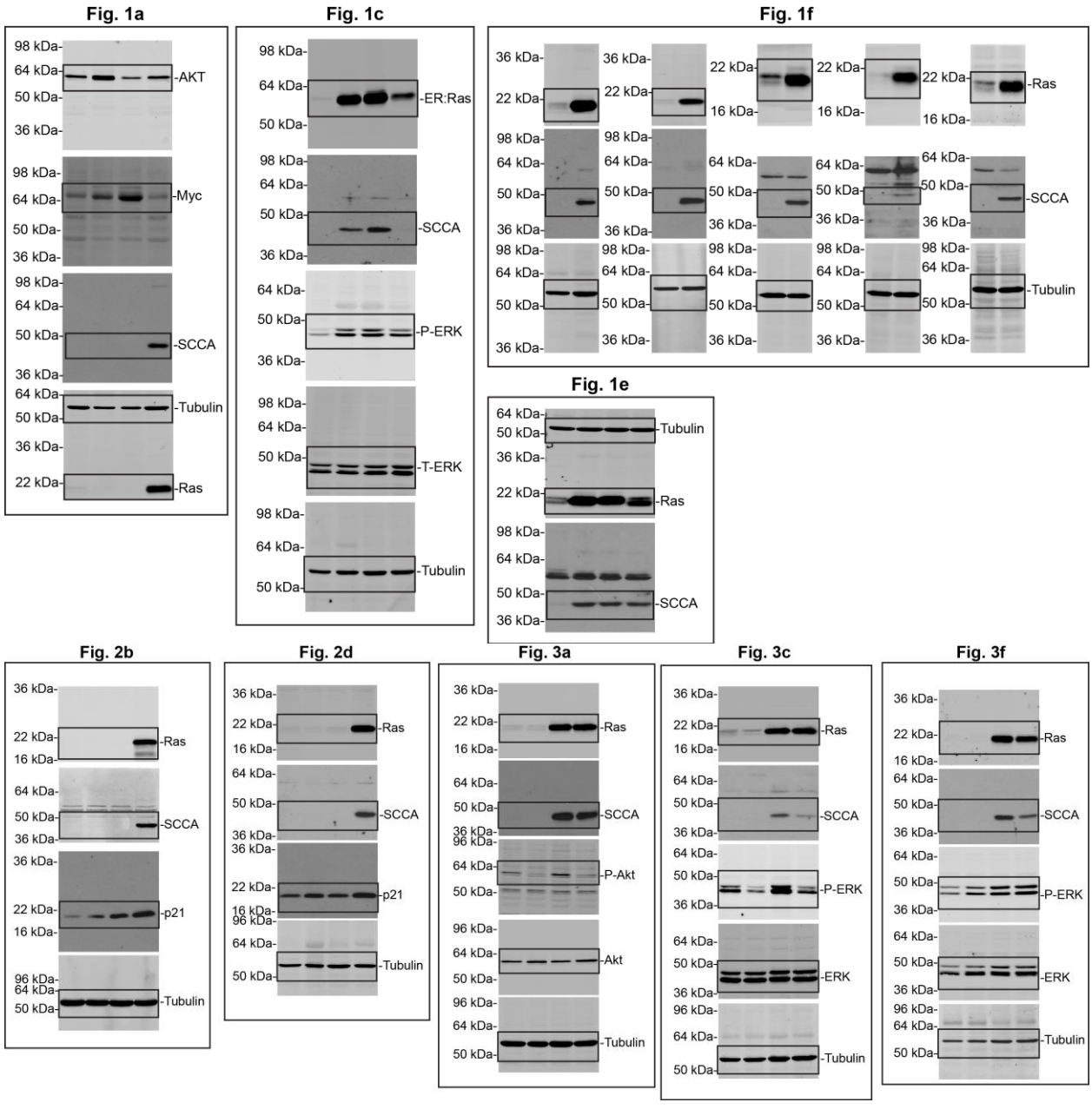
Supplementary Figure 6. SCCA positivity correlates with IL-6 expression in PanINs. (**a, b**) IHC against SCCA and IL-6 was performed on pancreatic tissue microarrays. (**a**) Representative images of serial sections of SCCA/IL-6-negative and SCCA/IL-6-positive samples are shown. (**b**) Quantification of IL-6 staining in SCCA-negative and SCCA-positive samples. Chi-squared test for trend was used to determine significance. Scale bar = 50μm; p = 0.0346.



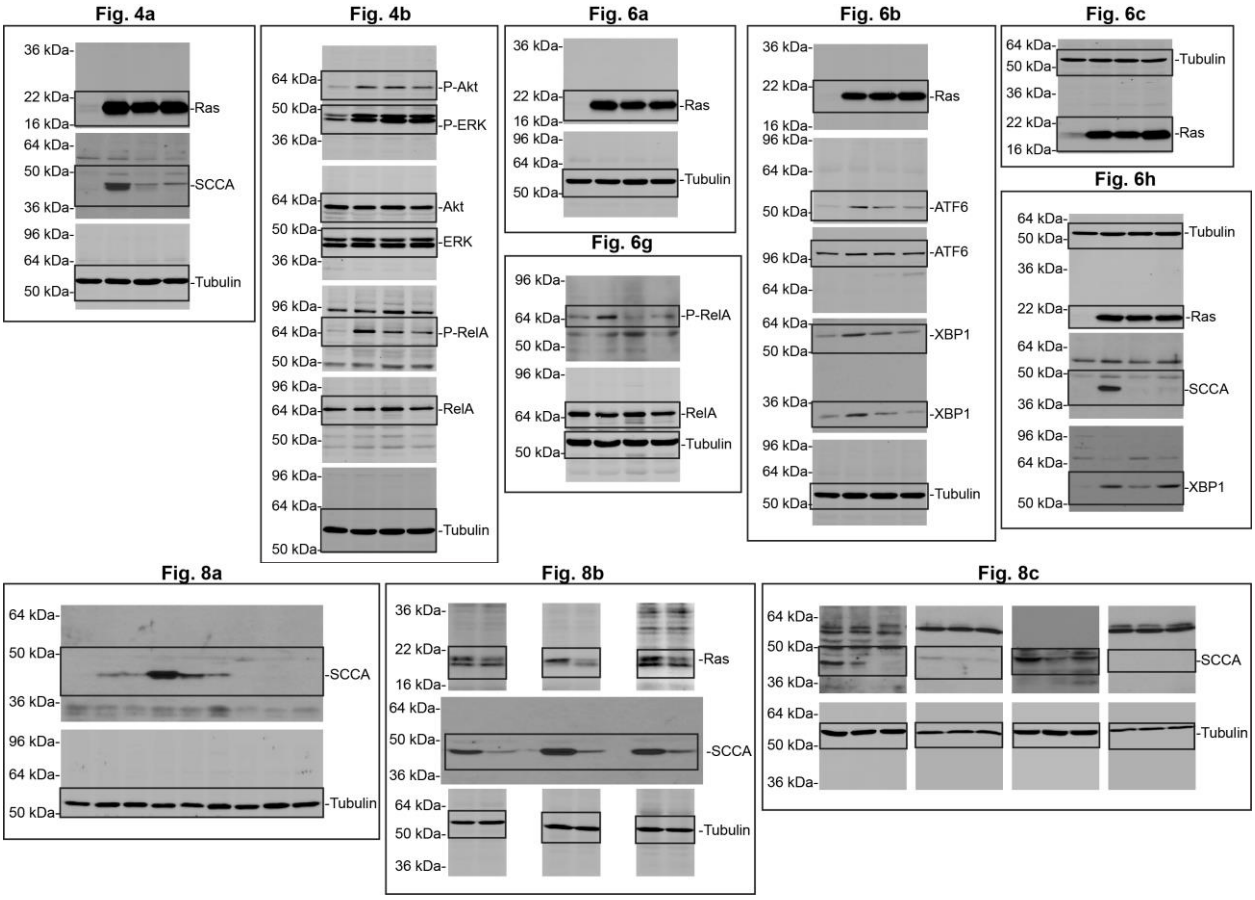
Supplementary Figure 7. Oncogenic Ras fails to induce Serpinb3a and Serpinb3b in murine cells. (**a**) NIH 3T3 cells stably expressing vector-control or $KRas^{V12}$ were harvested 7 d post-selection. Whole cells lysates and total RNA were obtained and analyzed by western blot with indicated antibodies or semi-quantitative RT-PCR for Serpin expression. Note that since antibodies against murine Serpinb3a and Serpinb3b are not available, semi-quantitative RT-PCR were performed. (**b**) Primary MEFs were stably transduced with vector-control and $HRas^{V12}$, and harvested 3, 5, and 9 d post-selection. Whole cell lysates and total RNA were obtained and analyzed by western blot with indicated antibodies or semi-quantitative RT-PCR for serpin expression. Serpinb3a and Serpinb3b expression constructs were used as positive controls for RT-PCR.



Supplementary Figure 8. SCCA silencing does not alter growth of pancreatic cancer cells *in vitro*. (**a-c**) Indicated cell lines were cultured in BrdU (10 μM) for 30 min and immunofluorescence against BrdU was performed. Quantification of percent BrdU-positive cells is shown. Cells were also cultured over 4 days and relative cell growth was quantified using crystal violet staining. Data shown are mean + SEM of two independent experiments. NS, non-significant by t-test.



Supplementary Figure 9. Full scans of immunoblots shown in figures 1-3.



Supplementary Figure 10. Full scans of immunoblots shown in figures 4, 6, 8.